pressure changes in the empty hemithorax. Furthermore, in light of the inherent weaknesses of the alternative options (ICT clamp–release, ICT to UWS, no ICT), a balanced drainage system appears most effective. This has been our clinical experience.

Previously, we mentioned that either a randomized, controlled clinical trial or an animal model would validate or repudiate our hypothesis and experience.[5] Pragmatism suggests that such a clinical trial, although desirable, is unlikely. On the basis of our clinical experience and these experiments, we continue to advocate managing the empty hemithorax after pneumonectomy with a balanced drainage system.

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Discussion

Dr Mark K. Ferguson *(Chicago, Ill).* Alvarez and coauthors are to be congratulated on a unique study that I think was carefully conducted on an important clinical problem. This complication doesn't happen commonly, but it is quite lethal when it does occur. As far as I can tell, this is the first experimental study to attempt to assess the role of pleural space drainage techniques in the etiology of this disorder. The results provide interesting, albeit preliminary, insights into the potential pathophysiology of this problem.

Dr Alvarez, in your initial experiment in which all animals underwent pleural drainage at 5 kPa pressure, there was a 60% rate of clinical respiratory distress. I understand that you think that this model is a somewhat typical clinical situation, but the extreme mediastinal deviation that you describe is not typical of the clinical situation, and by my calculation the 5 kPa is equivalent to more than -50 cm H_2O suction. Now, could that amount of shift cause a substantial decrease in venous return, elevated venous pressure, and decreased lymphatic drainage from the lung? If so, this problem may be unrelated to hyperexpansion and so-called volotrauma.

In the second experiment, in which you used several different drainage techniques, there were several shortcomings that you yourself mentioned. It isn't intuitively obvious to me why lack of drainage leads to lung overexpansion. So I wonder whether there were clinical findings in these animals that could suggest a method for mediastinal shift and hyperinflation of the remaining lung, such as extensive subcutaneous emphysema. Similarly, when you unclamped the UWS periodically, did those animals exhibit a large amount of air flow through the chamber when that occurred?

In assessing the pulmonary edema, although the histologic method you described has been standardized through a number of decades, I'm wondering whether you considered correlating these findings with some other way of measuring lung water, such as wet weight/dry weight ratios.

Your findings are intriguing and provide a possible insight into the clinical observation that balanced drainage is a superior technique for managing the postpneumonectomy space. I encourage you to refine the technique to better explore this problem.

Dr Alvarez. Thank you for those kind comments. Yes, 5 kPa is about 50 cm H_2O. It's extreme. The whole point was to show that this actually could cause PPE. The whole idea of doing a right pneumonectomy and so forth was to give ourselves the best opportunity to see this. We faced tremendous criticism in doing these experiments, causing tremendous emotional and psychologic disturbance to the sheep's well-being, and the idea of doing an

experiment in which an animal is supposed to get sick is difficult to get through the ethics committee.

Why 5 kPa was really quite simple. At 5 kPa, the tubes collapsed. We couldn't go any higher. I think we're fortunate that the sheep have a tremendous mesentery between the inferior vena cava and the mediastinum. It's about 4 or 5 cm there. We really didn't know when we applied it whether we would have hemodynamic collapse and so forth, and we had to do a pilot study and so on. It doesn't happen. They cope with it remarkably well.

You comment on the lymphatics and the effects of right ventricular dysfunction, and you are quite right. These are potential confounding variables. But I think that what we showed was that in a young, healthy, sheep without exposure to cigarette smoke, you apply 5 kPa of suction (and it may actually only take 3 kPa or 2 kPa) to inflate that lung, and 6 of 10 sheep get sick and have PPE develop.

As to, why lack of drainage is associated with PPE, I suspect a possible reason is that if air comes out of a thoracic cavity, the most likely source is the chest, which can lead to mediastinal shift. You can have massive volume changes. And I suspect that may well be the case in our patients. They cough, they expectorate, all those things, and some air may move. I suspect that's the actual issue there. Air escaped. There is not a hermetic seal. Things change.

When we looked back, all of our cases of PPE had subcutaneous emphysema. As to whether I can correlate that with our sheep, it's quite hard to do, and I'm afraid I just couldn't do it. That's one of the limiting factors. How much air came out of the chest tube when we clamped and released the thing was impossible to determine. I couldn't do it all the time by myself. I had to rely on animal technicians and so on and so forth. I thus can't quantify that. There are certain limitations.

The right/left ratios weren't going to tell us much, because I was constrained by the ethics committee. The sheep had to be killed on day 5. Now, if I could examine these rations when there was a fatality, then we might be able to show something. So with these right/left ratios, there was no correlation. If the triggering event occurred, say, 24 hours before the animal was killed versus 2 or 3 days, you would have substantial differences with those right/left ratios.

Dr Frank Detterbeck *(New Haven, Conn).* I commend you on a great study and taking this issue to the laboratory to try to understand this. If we look in the literature and at our clinical experiences, there is also an incidence of unexplained pulmonary edema that occurs after less serious resections than pneumonectomy, such as after a lobectomy and even occasionally after a wedge resection. Furthermore, if you look at an extended pneumonectomy, such as a carinal sleeve pneumonectomy or something like that, the incidence is higher than for simple pneumonectomy. So the incidence seems to correlate with the magnitude of the operation. I'm having a hard time explaining pulmonary edema in the setting of a lobectomy by your findings regarding hyperinflation. Do you have thoughts regarding that?

Dr Alvarez. In our first article, 1 of the patients actually had undergone a lobectomy. It was a lower lobe, and a very big lower lobe at that. I think it doesn't happen as much with a lobectomy simply as a volume issue. But if you get the right circumstances, such as a large lower lobe and thus a potential space, it doesn't take much to push these patients over the edge. Their lymphatics may be interfered with, right ventricular dysfunction can occur, they are all smokers, and so on. We already know from Waller's experience that the lungs are leaky after pneumonectomy. If you add another insult in our patient population and somehow disrupt that alveolar epithelial membrane in whatever way, it's like a crack in a dam. So you get the right patient with a large lower lobe that you have taken out, and there's a potential space there. You have set yourself up for it. Now, a balanced drainage system is one way of alleviating this. This is a minute-by-minute, instantaneous measurement.